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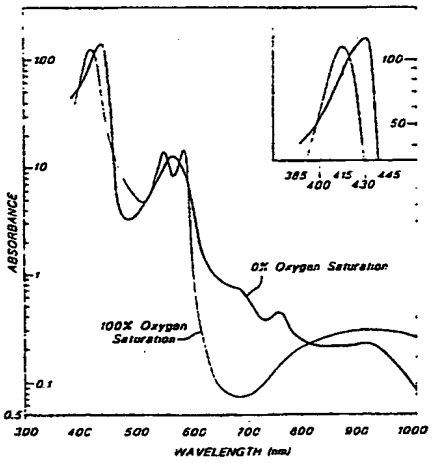
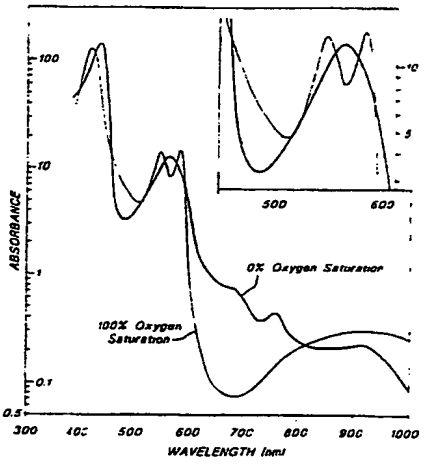
(54) Title: OXIMETERS





(57) Abstract

An oximeter technique, that is measuring the oxygen saturation of blood of a subject, including examining the absorption characteristic of said blood on a nanometric basis over a wavelength range within the range of 350 to 600 nanometers, determining the nanometric specific absorption charact ristic and directly from the wavelength shift of said specific absorption characteristic from the known physiological endpoints the actual oxygen saturation percentage.

* See back of page

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OXIMETERS

This invention relates to oximeters, devices to measure the oxygen saturation of blood.

Such devices have great value to medical practitioners in providing an indication of the oxygenation of the blood of a patient. Present devices, while of substantial assistance, can be adversely affected by many sources of error because of the assumptions that are made in interpreting the results of the measurement techniques.

Many present devices, generally known as pulse oximeters, use radiation at two or more wavelengths, one in the red region (650 to 750 nanometers) and another in the infra-red region (above 750 nanometers). The measurements of detected transmitted or reflected intensities are compared on the basis of the Lambert-Beers transmittance law to estimate oxygen saturation. Such comparative measurements are prone to error for various reasons:-

i. Changes in the optical properties of skin with time.
ii Beers Law not always obeyed.
iii Unknown and variable blood content in the light path.
iv. Unknown mixture of arterial and venous blood in the light path.
v. Poor peripheral circulation.
vi. Effects due to multiple scatter.
vii. Abnormal blood pH.
viii. Movement artefacts.
ix. Non-monochromacity and stability of (LED) light sources.
x. Errors in hypoxia.
xi. Location limitation.
xii. Ambient light and infra-red radiation.
xiii. Other haemoglobin derivatives e.g. fetalhaemoglobin methaemoglobin, carboxyhaemoglobin.

While acceptable corrections can be made for these sources of error such corrections add to cost and complexity and overall there is an adverse effect on the utility of the measurement.

Also various specific proposals have been made to determine haemoglobin concentration. Thus Reeves, Respiration Physiology, Vol. 42, No. 3, December 1980 (Netherlands/Elsevier) pages 299-315 uses a cell containing a blood sample film and controls the oxygen tension around the blood film. Two discrete wavelengths are used, in the conventional way, but instead of the usual red and infra-red wavelengths one of the two Soret absorbtion peak wavelengths and an adjacent isosbestic wavelength are used to give the basis for the conventional ratiometric measument. DE-A-3615973 shows a technique for measuring the haemoglobin concentration, without distinguishing whether oxyhaemoglobin or reduced haemoglobin was originally present. As much haemoglobin as possible is converted to oxyhaemoglobin by sufficient oxygen and the concentration of this converted material measured using the appropriate Soret wavelength, i.e. 415 nanometres. In DE-A-3700577 a general investigative technique is exemplified by a specific form stated to be suitable for the determination of the oxygen saturation of arterial blood. Measurements of light from a continuous spectrum light source of standard characteristics transmitted through a sample under investigation are made using two photodetectors having different but overlapping spectral characteristics in the visible light range. The outputs of the photodetectors are divided one into the other and the quotient used to produce a "colour value" for the sample. It is stated that this "colour value" can provide information about the sample by using the ratiometric colour value to derive physical data from a look-up table. For example it is stated that the colour value of a blood sample can give information about oxygen saturation of blood by being accurately indicative of the transmission wavelength. No specific wavelengths for the photodetectors are given. The quotient of the two photodetector outputs is the significant signal from the essentially comparative technique.

Comparison of output signals to produce a potentially useful value is the basis of all the above techniques which can suffer from various defects as set out earlier.

It is an object of the present invention to avoid these adverse effects by applying a fundamental measurement technique.

According to one aspect of the invention there is provided a method of measuring the oxygen saturation of blood of a subject including examining the absorption characteristic of said blood on a nanometric basis over a wavelength range within the range of 350 to 600 nanometers, determining the nanometric specific absorption characteristic and directly from the wavelength shift of said specific absorption characteristic from the known pysyiological endpoints the actual oxygen saturation percentage.

The method may include directing the light along blood measurement and reference paths, selecting the light from said paths in turn, and applying the selected light to an optical detector. The blood may be in the subject or as a sample.

The method may include varying the wavelengh of the light on a nanometric basis or illuminating the blood with a band of wavelengths of light, dispersing the light from the illuminated blood as a spectrum and examining the spectrum for said wavelength shift of said characteristic.

According to another aspect of the invention there is provided an oximeter including means to provide light in a band of wavelengths at least over a range lying within 350 to 600 nanometers, means to apply said light to a blood measurement path, means to disperse light received from said path as a spectrum and means to detect light of said spectrum to determine the specific absorption characteristic of the blood measurement path and means to indicate from the nanometric shift of said characteristic the oxygen saturation of blood in said blood measurement path.

According to yet another aspect of the invention there is provided an oximeter including means to provide light of a wavelength nanometrically controllably variable within a range between 350 to 600 nanometers, means to apply said light of controllably variable wavelength to a blood measurement path, means to detect light received from said path and determine the specific absorption characteristic of the blood measurement path and means to indicate from the nanometric wavelength shift of said characteristic the oxygen saturation of blood in said blood measurement path.

The light may be applied over distinct paths in turn to said detector or examined in any convenient way to provide absorption wavelength information.

The oximeter may include means to apply said light to a blood measurement path and to a reference path not including blood for measurement and means to apply light from said paths in turn to said means to detect light for comparative detection. The means to apply light in turn may include a mechanical or other light beam chopper. The oximeter may include a light source of known intensity/wavelength characteristic to avoid the need for comparative detection.

The technique uses the direct relation of the wavelength shift of the absorption peak of the Sorét spectrum with oxygen saturation percentage change.

In a preferred arrangement according to the invention the absorption wavelength is determined by the method of tangents applied to the absorption characteristic in one of the ranges between known physiological endpoints 400 to 450, 465 to 520 and 530 to 600 nanometers and more specifically 410 to 440, 470 to 515 and 540 to 570 nanometers respectively.

Conveniently the method of tangents, or other appropriate analysis of the absorption spectrum, is carried out in a microprocessor. While ratiometric techniques may be more convenient for some uses absolute measurement is possible given sufficient stability of wavelength information.

In a further preferred arrangement the wavelength range 400 to 600 nanometers is used to assist in measurements through a fingernail. Optical fibres may be used to apply light to blood through the fingernail and receive light back from said blood.

The arrangement may include a probe to enable measurement in a subject including means to introduce optical fibres, ends of which respectively emit light to blood in the subject and receive light from said blood.

It is noted that oxygenated blood is also known as oxyhaemoglobin, HbO_2, and blood with no oxygen as reduced haemoglobin, Hb.

Embodiments of the invention will now be described with reference to the accompanying drawings in which:

Figures 1a, 1b show the accepted characteristic of variation of the light absorbance of blood with wavelength for oxygen saturation at 100% and 0%, and ,in detail enlargements, parts of the characteristic of relevance in understanding the invention,

Figure 2 shows in block schematic form an oximeter according to the invention,

Figure 3 and 6 shows graphs useful in understanding the invention, and

Figures 4 and 5 show arrangements for applying an oximeter according to the invention to a patient.

Figure 2 shows in block schematic outline the elements of an oximeter to measure oxygen saturation of blood when the blood is available as a sample.

Light from a source 10 such as a quartz-halogen lamp is supplied to a scanning monochromator 11, such as a Mini-chrom 1 from the supplier **ptr optics** of the USA. The scanning monochromator should be operable to produce light output to nanometric accuracies in the range 350 to 600 nanometers or selected parts thereof and this can be achieved by incorporating within the monochromator an optical grating with the efficiency maximised over the range 330 to 600 nanometers, or appropriate parts.

The supply to the lamp is stabilised and the lamp and monochromator together provide a source of monochromatic radiation whose bandwidth is defined by the physical parameters of the monochromator. A bandwidth less than 4 nanometers and preferably less than one nanometer is suitable, although a bandwidth less than 0.5 nanometer may be desirable in some cases. The monochromator has a control connection 12.

The nanometric light from the monochromator 11 is applied to a first beam splitter 21 which provides two output beams, one 27 as a reference the other 28 for application to a sample in holder 22. Mirrors 23, 24 conveniently return the reference output to a further beam splitter 25 acting to bring into a common path the reference 27 and beam 29 of the light of beam 28 which has passed through the sample holder 22. A beam chopper 26 is arranged to chop the beams synchronously so that phase sensitive detection can be used.

An optical detector 31 detects the intensity of the light emerging from the beam splitter in the common path and the detector output is supplied via a lock-in amplifier 32, coupled by connection 33 to the beam chopper 26, to a microprocessor 34. The microprocessor is connected to the scanning monochromator by two-way connection 12.

Alternatively an ultra-stable optical source can be used to avoid the need for a reference channel and an optical chopper to produce it. The radiation characteristic of the source is stored within the microprocessor memory and is used to compensate the measurements.

By correlating the operation of the monochromator 11 and the output of the detector 31 the wavelength at which the absorption of a sample in holder 22 is at a maximum or a minimum can be determined.

Another embodiment of the invention will now be described by reference to modifications to the Figure 2 arrangement. In Figure 2 omit items 11 and 34 and replace item 31 with a dispersive device such as a prism or a diffraction grating and a linear detector in the form of a charge coupled device to respond to the spectrum produced by the dispersive device. An optional band pass filter may replace item 11. Operation is as follows. Light from source 10, the quartz-halogen lamp, is supplied, through the optional band pass filter if used, to a first beam splitter 21 which provides two output beams, one 27 as a reference the other 28 for application to a sample in holder 22. Mirrors 23,34 conveniently return the reference output to a further beam splitter 25 acting to bring into a common path the reference 27 and beam 29 of the light of beam 28 which passed through the sample holder 22. A beam chopper 26 is arranged to chop the beams synchronously so that phase sensitive detection can be used.

Light emerging from the beam splitter in the common path is incident on the dispersive device and emerges as a optical spectrum alternately related to the material in the sample holder and to the reference beam. The spectrum so formed is arranged to fall onto the elements of the charge coupled device (CCD) array with the bluest wavelength at the first element and the reddest wavelength at the last element (or vice-versa). The CCD is scanned from the first element to the last element to collect information about the optical spectrum. This scanning is conveniently performed under the control of a microprocessor via a suitable circuit link and the element information is returned to the microprocessor via another circuit link. The whole procedure is synchronised by the microprocessor to the beam chopper 26 via link 33 in order to produce sample and reference spectra information.

Alternatively, as before, an ultra-stable optical source can be used to avoid the need for a reference channel and an optical chopper to produce it. The radiation characteristic of the source is stored within the microprocessor memory and is used to compensate the measurements.

Algorithms within the microprocessor provide means for the determination of the specific absorbtion wavelength of the sample in the sample holder 22 for the shift of the specific absorbtion characteristic in the range of the known physiological points.

It has been found, as shown in Figure 3, that the oxygen saturation of blood is related to the wavelength of peak absorption in the Sorét region range, 400 to 450 nanometers. As seen in the insert to Figure 1 there are distinct peaks of the absorption characteristics at 0% and 100% oxygen saturation. The presence of these distinct peaks produces an identifiable variation in absorption with oxygen saturation. Accordingly from the determination of absorption peak in this range the oxygen saturation can be assessed and indicated by a rapid simple measurement of a sample. The graph in Figure 3 relates to a particular method of determining the peak and thence the oxygen saturation percentage which has been found to be convenient. Clearly other graphs may relate to other methods but such variations do not go beyond the scope of the invention. The method employed is the method of tangents where the tangents to the points of inflection of the absorption characteristic on each side of the absorption peak are used to indicate by their intersection the wavelength for the peak. Thus the "peak" need not be the peak in visual terms but is a repeatably determinable parameter of the particular type of instrument used to embody the invention. The regions 465 to 520 and 530 to 600 nanometres have similar distinct peaks, or troughs, in the characteristics and therefore the ability to provide the identifiable variation in absorption with saturation as a repeatable parameter. Figure 6 shows a graph similar to Figure 3 but for the trough region 480 to 500 nanometres.

The techniques for securing and handling the sample are well-known and should be applied. A removable optical cuvette can be used for a static sample while a column can be used for the continuous flow of a sample.

In the arrangement described so far the light is passed through a sample in a holder, i.e. an in vitro technique. For medical use it is convenient to avoid the need to take a sample from a patient, that is techniques known respectively as non-invasive and in vivo.

Figure 4 shows in outline apparatus by which the arrangement of Figure 2 can be coupled to a patient without penetration of the skin. The apparatus in Figure 4 replaces the optical chamber 22 of Figure 2. Light from beam 28 is directed by a mirror 41 along a fibre optic 43. A holder 45 is arranged to position fibre optic 43 over a finger or toe nail essentially normal thereto to direct light beam 48 through the nail. A further fibre optic 44 is positioned by holder 45 to collect light from fibre optic 43 reflected, as indicated generally at 49, from the capilliary bed. Light collected by fibre optic 44 is directed by mirror 42 towards the beam chopper 26 and thence to the rest of the Figure 2 arrangement.

Figure 5 shows in outline apparatus by which the arrangement of Figure 2 can be coupled to a patient and applied to a vein, artery or organ by puncture. In place of the fibre optics and holder (43, 44, 45) of Figure 4 is a structure 51, like a hypodermic needle or indwelling flexible catheter, which houses two fibre optics 52, 53. Generally the structure 51 is arranged to puncture the skin and take the output and input ends of fibres 52, 53 to the region of interest. Light 58 emerging from fibre optic 52 returns from the area of interest as light 59 for collection by fibre optic 53. Elements 28, 41, 42 and 26 are as described above.

The general techniques for the above devices will be readily apparent to those skilled in the art and will not be described further.

As mentioned above microprocessor control is used. Typically arrangement and operation is as follows.

The instrument is run under microprocessor control. The scanning monochromator is driven by a stepper motor and gearbox assembly. The microprocessor monitors the position of the grating, and hence the wavelength of light produced, and correlates this information with the digitised signal obtained from the optical detector. All this information is then stored as a bit pattern in a random access memory (RAM). There can be a digitised scan of the optical detector output searching for a peak (maximum or minimum).

The mathematical operation, already described, to establish the wavelength of peak absorption (maximum or minimum) is contained within the software of the microprocessor. Data relating to the spectral calibration characteristics of the blood is stored in memory within the instrument. When the calculations on the sample have been completed the peak wavelength value is then used as a pointer in a look-up table to establish the oxygen saturation of the sample. Using a variety of calibration parameters stored in a look-up table allows the instrument to be flexible so that depending on the clinical situation the most appropriate characteristic or group of characteristics can be chosen to produce statistically the best reading for oxygen saturation. Furthermore the availability of several regions where oxygen saturation can be measured permits cross-checks and possible improvements in accuracy.

Optical reference points are provided within the monochromator scanning system by inclusion of one or more standard wavelength sources. These allow the microprocessor to calibrate the monochromator.

In principle, this instrument may incorporate measurement circuits, sensors and algorithms based on existing technology to measure other parameters in the sample such as pH, pCO_2 and other haemoglobin derivatives. This, in addition to the scanning elements outlined above, would lead to a comprehensive instrument that could be used as a laboratory standard.

It is important to note that the improvements provided by the present invention result from the direct, fundamental measurement of oxygen saturation possible by measuring the peak absorption wavelength (maximum or minimum) rather than by relying on the derivative techniques used before.

CLAIMS

1. A method of measuring the oxygen saturation of blood of a subject including examining the absorption characteristic of said blood on a nanometric basis over a wavelength range within the range of 350 to 600 nanometers, determining the nanometric specific absorption characteristic and directly from the wavelength shift of said specific absorption characteristic from the known pysyiological endpoints the actual oxygen saturation percentage.

2. A method according to Claim 1 including directing the light along blood measurement and reference paths, selecting the light from said paths in turn, and applying the selected light to an optical detector.

3. A method according to Claim 1 including providing the blood in the subject or as a sample.

4. A method according to Claim 1 including varying the wavelengh of the light on a nanometric basis.

5. A method according to Claim 1 including illuminating the blood with a band of wavelengths of light, dispersing the light from the illuminated blood as a spectrum and examining the spectrum for said wavelength shift of said characteristic.

6. An oximeter including means to provide light in a band of wavelengths at least over a range lying within 350 to 600 nanometers, means to apply said light to a blood measurement path, means to disperse light received from said path as a spectrum and means to detect light of said spectrum to determine the specific absorption characteristic of the blood measurement path and means to indicate from the nanometric shift of said characteristic the oxygen saturation of blood in said blood measurement path.

7. An oximeter according to Claim 6 in which the light is dispersed by a diffraction grating and detected on a row of elements in a charge coupled device.

8. An oximeter according to Claim 6 in which the range for said band of wavelengths is set by a band pass filter.

9. An oximeter including means to provide light of a wavelength nanometrically controllably variable within a range lying within 350 to 600 nanometers, means to apply said light of controllably variable wavelength to a blood measurement path, means to detect light received from said path and determine the specific absorption characteristic of the blood measurement path and means to indicate from the nanometric shift of said characteristic the oxygen saturation of blood in said blood measurement path.

10.An oximeter according to Claim 9 in which the light is applied over distinct paths in turn to said detector to provide absorption wavelength information.

11.An oximeter according to Claim 9 including means to apply said light to a blood measurement path and to a reference path not including blood for measurement and means to apply light from said paths in turn to said means to detect light for comparative detection.

12.An oximeter according to Claim 11 in which the means to apply light in turn include a mechanical or other light beam chopper.

13. An oximeter according to Claim 9 including a light source of known intensity/wavelength characteristic to avoid the need for comparative detection.

14. An oximeter according to Claim 9 including means to apply light from said source and direct it in vivo through the blood of a subject and means to collect light passed throgh said blood in vivo for determination of said wavelength shift.

15. A method of measuring the oxygen saturation of the blood of a subject from the direct relation of the wavelength shift of the absorption peak of the Sorét spectrum with oxygen saturation percentage change.

16. A method according to Claim 1 or Claim 15 including determining the wavelength of the specifc absorption characteristic by the method of tangents applied to the absorption characteristic in one of the ranges betwen known physiological endpoints 400 to 450, 465 to 520 and 530 to 600 nanometers and more specifically 410 to 440, 470 to 515 and 540 to 570 nanometers respectively.

17. A method of measuring the oxygen saturation of the blood of a subject substantially as herein described with reference to the accompanying drawings.

18.An oximeter substantially as herein described with reference to the accompanying drawings.

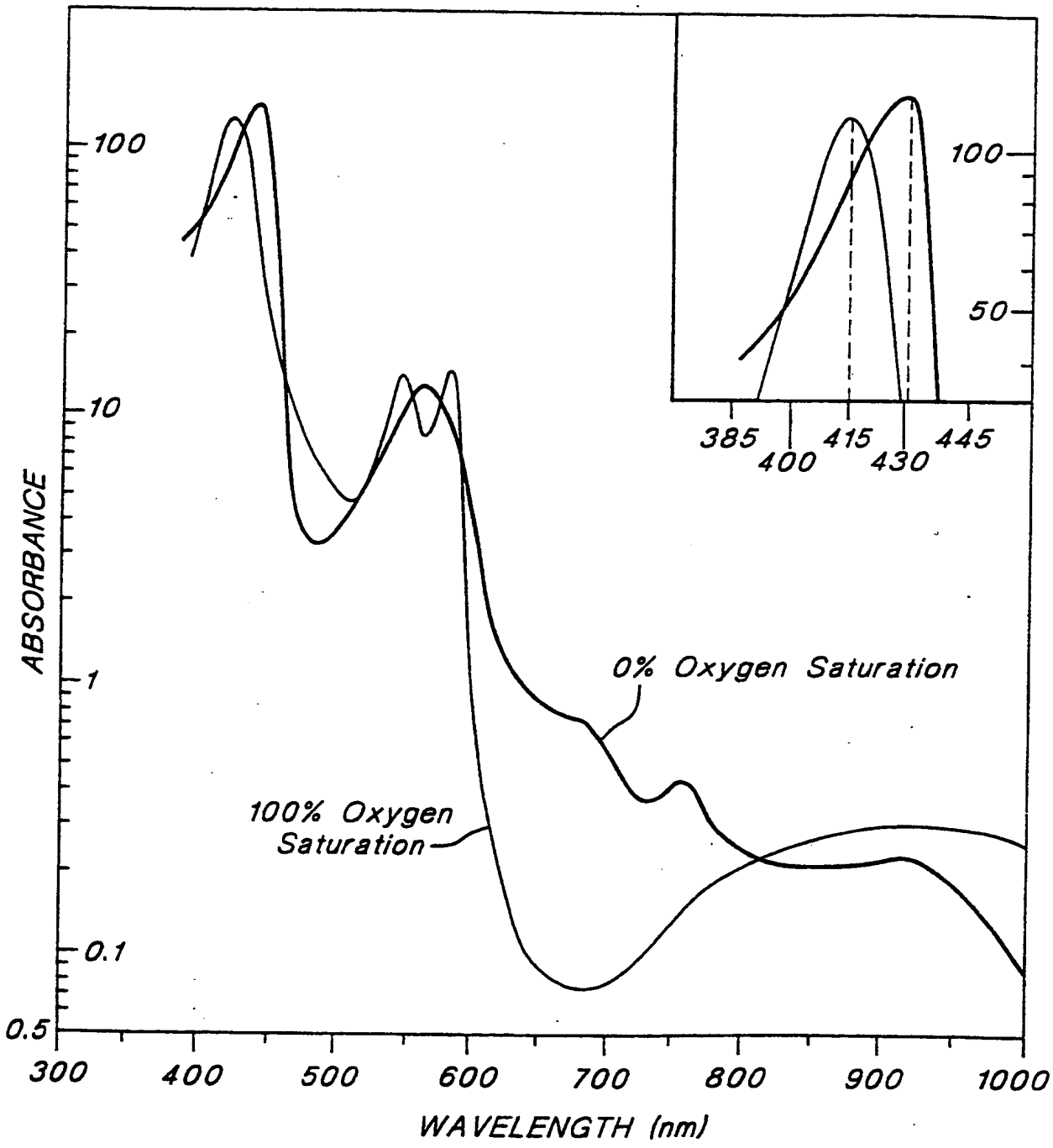

Fig. 1a

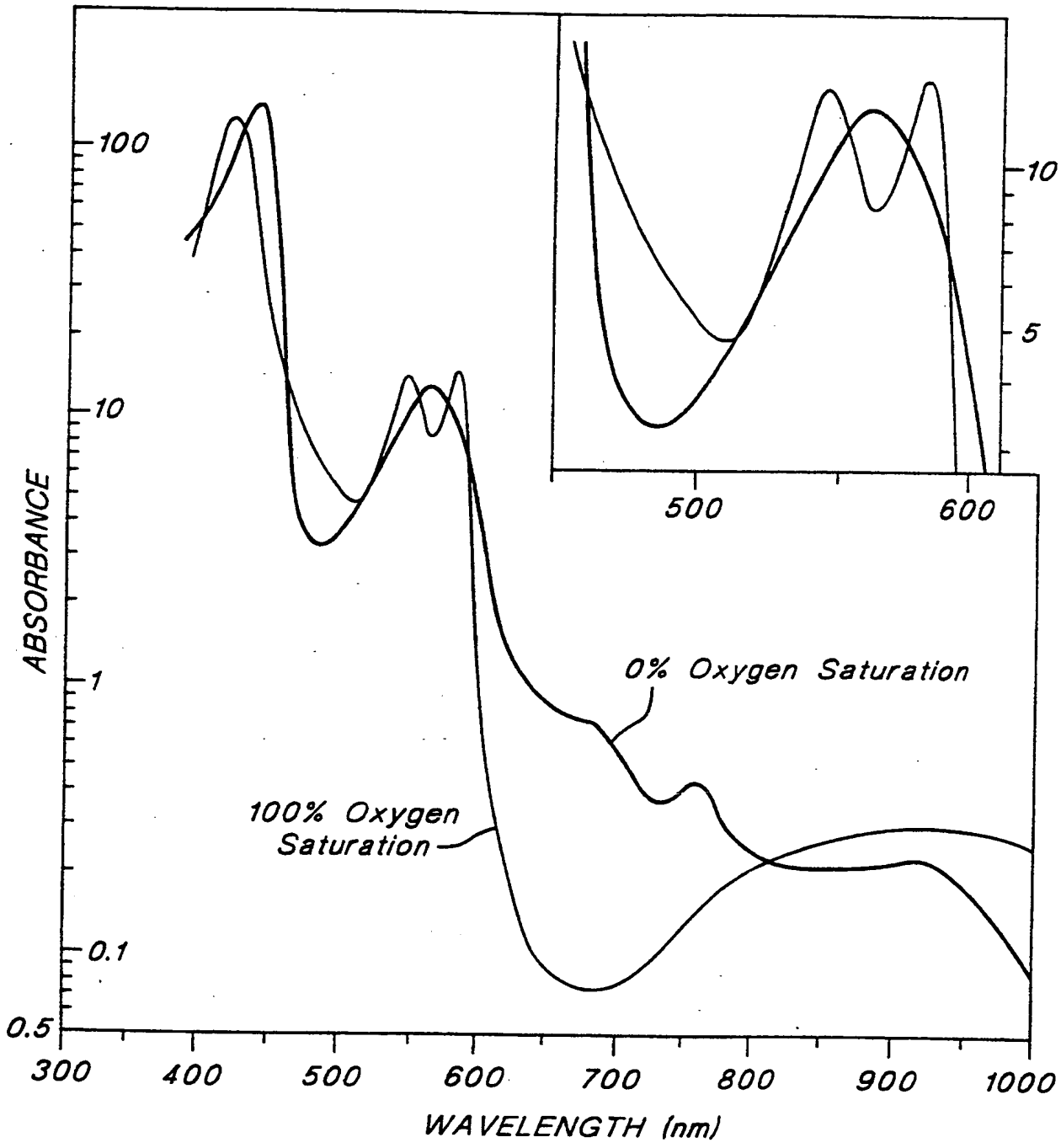

Fig. 1b

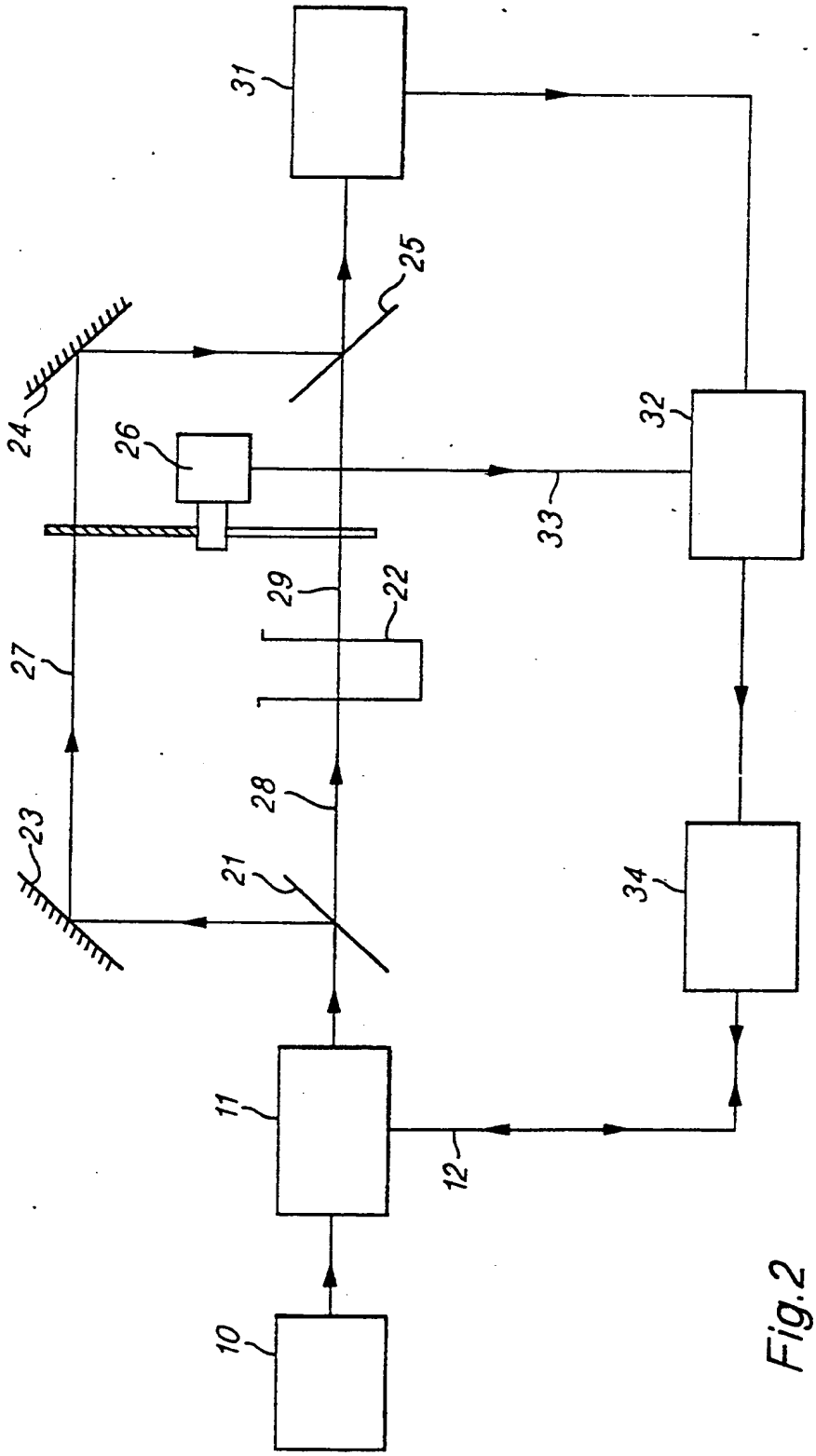

Fig.2

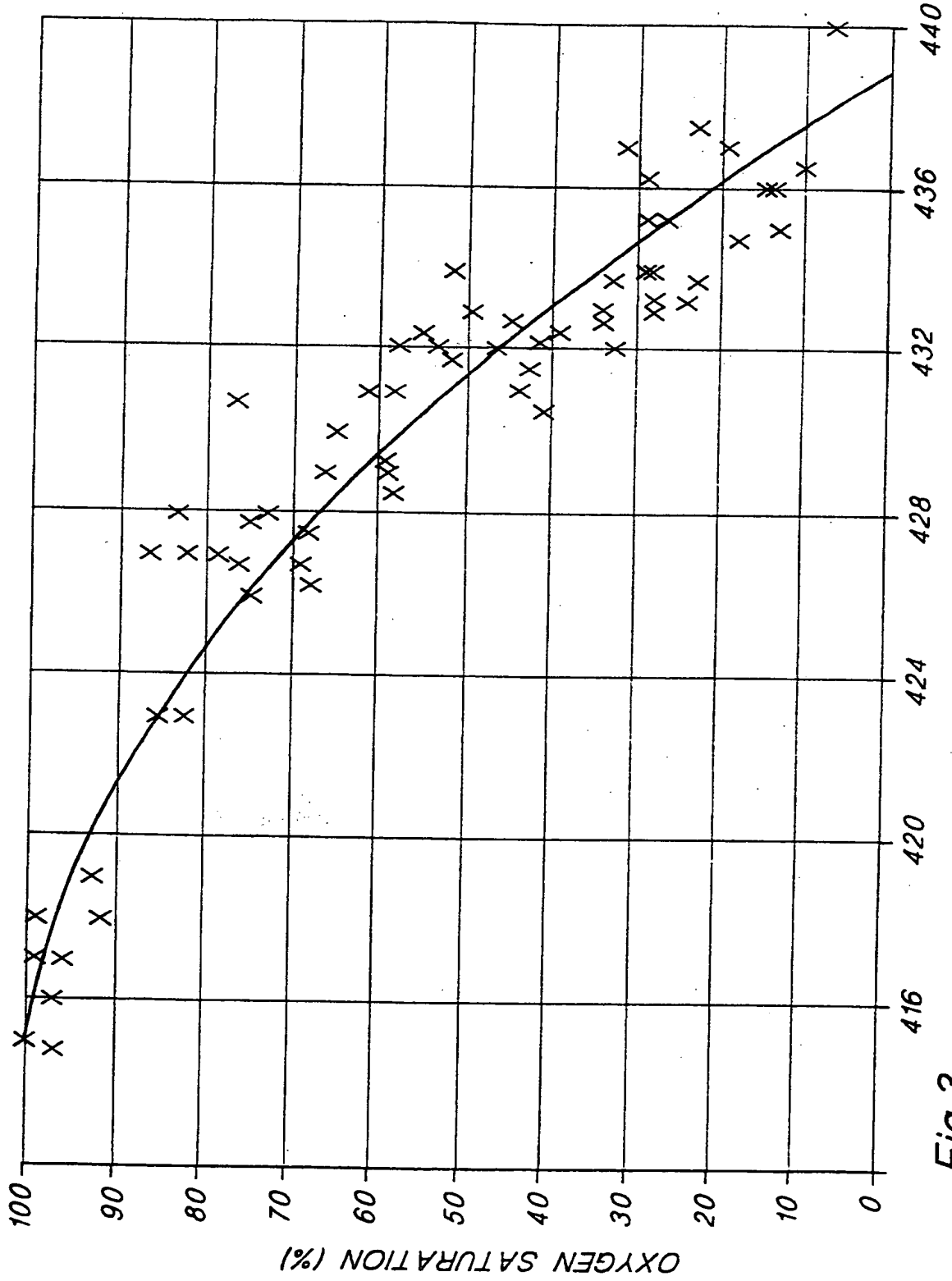

Fig.3

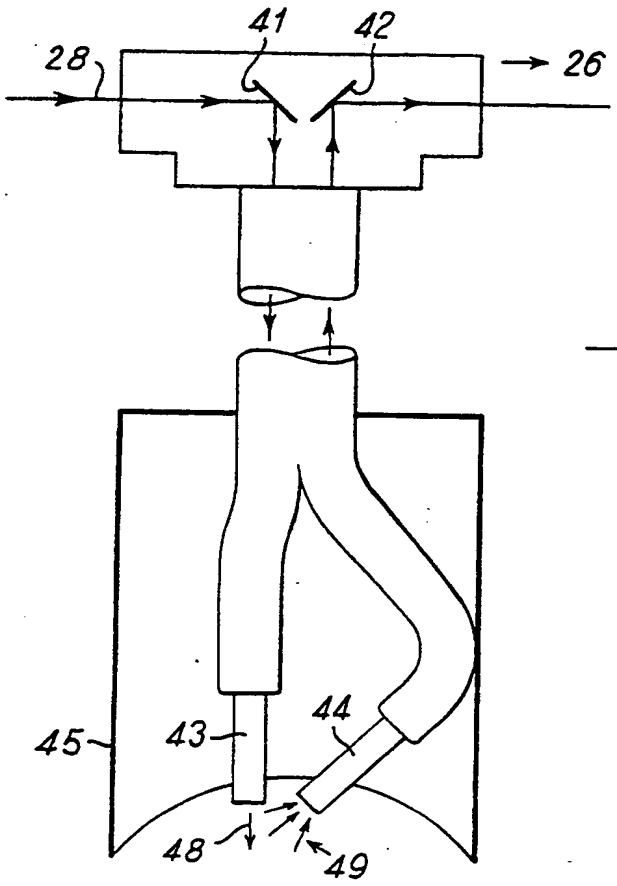

Fig. 4

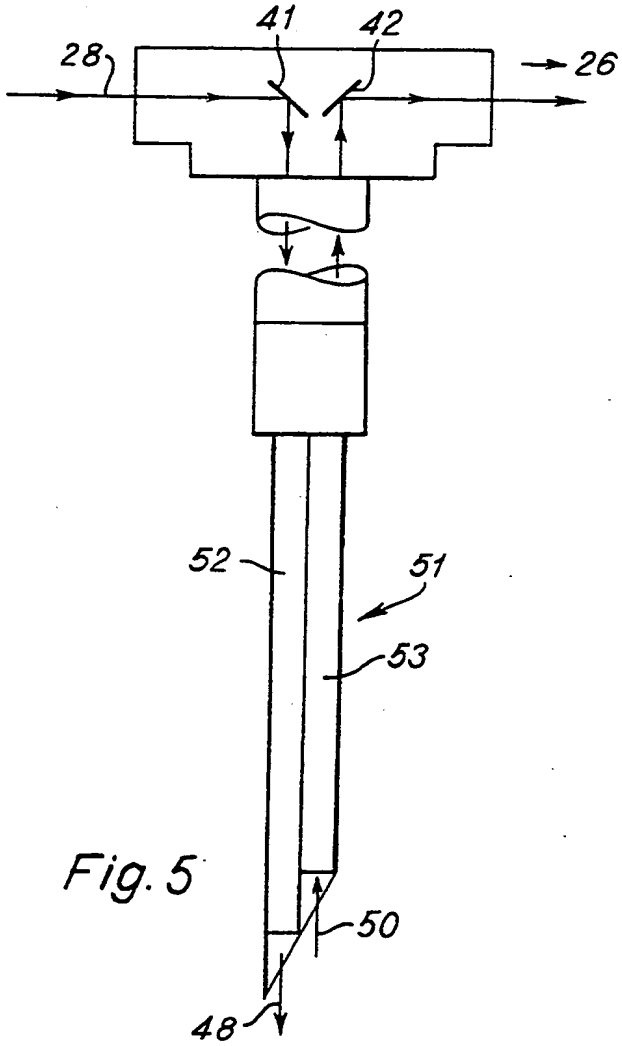

Fig. 5

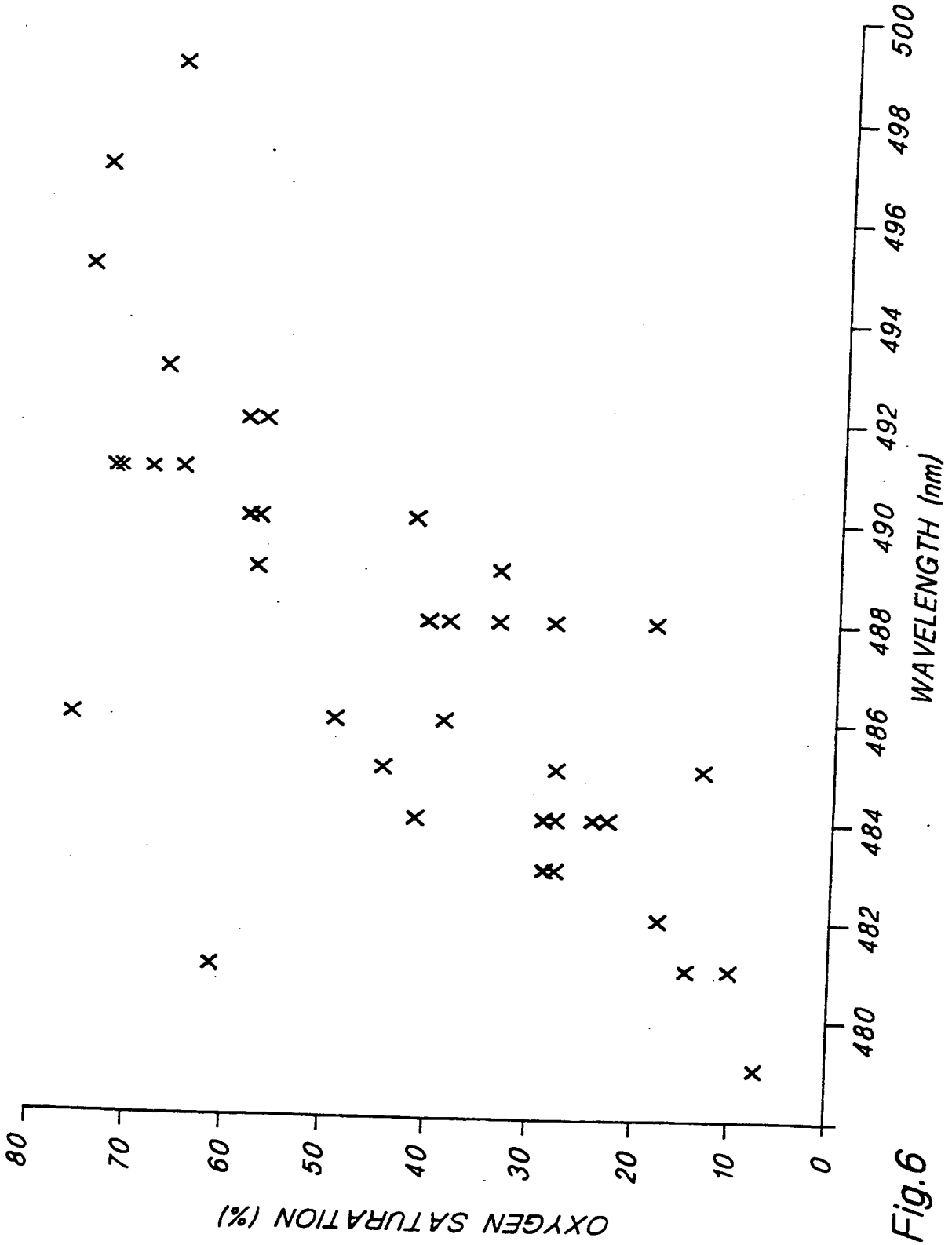

Fig.6

INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 90/01170

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 A61B5/00

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	A61B ; G01N ; G01J

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
A	RESPIRATION PHYSIOLOGY Vol. 42, no. 3, December 1980, NL pages 299 - 315, REEVES: "A rapid micro method for obtaining oxygen equilibrium cruves on whole blood." see pages 302 - 304, section "Measurement of oxy-hemoglobin saturation." "document cited in the application"	1, 3-6, 9, 10, 13
A	DE,A,3615973 (STILLER) 19 November 1987 see abstract; figure see column 3, line 1 - column 4, line 15 "document cited in the application"	1, 3, 4, 6, 8, 9, 13
A	DE,A,3700577 (EICHHOLZ) 21 July 1988 see figures see column 9, line 44 - page 12, line 64 "document cited in the application"	1, 3, 5, 6, 9, 14

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° Special categories of cited documents :[10]

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

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"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
16 NOVEMBER 1990	23 NOV 1990
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	CHEN A.H. A Chen

Form PCT/ISA/210 (second sheet) (January 1985)

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	EP,A,280986 (SUMITOMO ELECTRIC INDUSTRIES) 07 September 1988 see figure 4 see column 4, line 42 - column 5, line 47	1-3, 5, 6, 9-11, 13, 14
A	US,A,3136310 (MELTZER) 09 June 1964 see figures 1, 3 see column 2, lines 3 - 41	1, 3-6, 9, 12-14
A	US,A,4060327 (JACOBWITZ ET AL) 29 November 1977 see figures see column 3, line 26 - column 4, line 58	5-7

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.

GB 9001170
SA 39303

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 16/11/90
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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DE-A-3700577	21-07-88	None	
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		JP-A,B,C 53036285	04-04-78

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